IN THE SPECIFICATION:

Please substitute the following replacement paragraphs:

[001] The present invention is directed to a viral vector that can introduce a desired nucleic acid sequence into a ~~targetted~~targeted host cell by retroviral infection where the nucleic acid sequence ~~repicates~~replicates episomally. Preferably, the viral vector is a lentiviral vector that also contains a heterlogous viral origin of replication (ori) and a second gene that functions as a replication transactivator.

[005] Recently, attention has ~~focussed~~focused on lentiviral vectors such as those based upon the primate lentiviruses, e.g., human immunodeficiency viruses (HIV) and simian immunodeficiency virus (SIV). HIV vectors can infect quiescent cells in addition to dividing cells. Moreover, by using a pseudotyped vector (i.e., one where an envelope protein from a different species is used), problems encountered with infecting a wide range of cell types can be overcome by selecting a particular envelope protein based upon the cell you want to infect. Moreover, in view of the complex gene splicing patterns seen in a lentiviruses such as HIV, ~~multivaliant~~multivalent vectors (i.e., those expressing multiple genes) having a lentiviral core, such as an HIV core, are expected to be more efficient. These vectors like MMLV also result in having the genetic material integrated into the host cell with high efficiency.

[008] Further, there are many instances where one does not want to have a gene stably integrated, but only expressed for a limited time period. For example, such as approach is useful with "suicide therapy" where the gene product is designed to negatively impact the integrity of the host cell. It is also useful with ~~angiogenes~~angiogenesis proteins. These proteins can promote wound healing, growth of blood vessels, etc. Thus, they can be useful in dealing with individuals having circulatory problems, heart problems etc. However, these proteins can also cause the growth of blood vessel regulated tumors. Accordingly, while some expression of the protein can be beneficial, its unlimited expression can ultimately cause more harm than benefit.

[010] We have now discovered a viral vector system that takes advantage of retroviral infection to bring a desired nucleic acid sequence to a ~~targetted~~targeted host cell without resulting in stable integration.

[017] In another embodiment the lentiviral vector is another form of self-inactivating (SIN) vector as a result of a deletion in the 3' long terminal repeat region (LTR). Preferably, the vector contains a deletion within the viral promoter. The LTR of lentiviruses such as the HIV LTR contains a viral promoter. Although this promoter is relatively inefficient, when *trans*activated by e.g. tat, the promoter is relatively efficient. However, the presence of the viral promoter can interfere with heterologous promoters operably linked to a transgene. To minimize such interference and better regulate the expression of transgenes, the ~~lentiviral~~lentiviral promoter is preferably deleted.

[026] The packaging vector also contains at least one component of the episomal replicon. Preferably, one uses a DNA viral replicon. DNA viruses that can be used include SV40 Epstein-Barr virus (EBV) and BK virus [Cooper, M.J., et al., *Proc. Natl. Acad. Sci. USA*, 94, *supra*; Eckhart, W., *Virology* 38:120-125 (1969); Asconzioni, F., et al., *Cancer Lett.*, 118:135-142 and Fried, M., *Proc. Natl. Acad. Sci. USA*, 53:486-491 (1965)]. The replicon comprises a viral DNA origin of replication (ori) and a protein that acts as a replication transactivator. Typically, that protein is an early gene product from the same virus. However, other constructs can be used. [See for example, Piechaczek, C., et al., *Nucleic Acids Research*, 27:426-428 (1999)]. Because the viral proteins such as large T-antigen for SV40, EBNA-1 for EBV, and large T-antigen for BK virus are transforming (i.e. tumorigenic), the use of modified constructs is preferred. For example, deleting domains that bind human tumor suppressor gene products such as p53, retinoblastoma and p107. One such construct is the SV40 mutant 107/402-T which encodes a lysine instead of glutamic acid at codon 107 and ~~glutanie~~glutamic acid

instead of aspartic acid at codon 402. Other amino acids can also be substituted. Binding activity can readily be determined in an *in vitro* assay by known means. Another construct that can be used instead of SV40 T-antigen is the S/MAR (scaffold/matrix attached region) fragment from a gene such as the human interferon β-gene.

[042] We have now discovered a viral vector system that takes advantage of retroviral infection to bring a desired nucleic acid sequence to a ~~targetted~~targeted host cell without resulting in stable integration.

[049] For example, we have shown that the 1-212 class II IN deletion mutant was not only replication-defective in highly permissive MT-4 cells (Fig. 1~~b~~c), but 1-212 carrying oriT did not detectably replicate in infected TAg-expressing 1D Jurkat cells (data not shown). These results highlight the advantage of creating a relatively unperturbed IN protein domain during HIV-1 particle assembly (Bukovsky and Göttlinger, 1996) for subsequent virus infectivity. However, by determining the domains necessary for viral replication for instance by creating a range of deletion mutants, one can readily determine which deletions one should not make.

[052] In another embodiment the lentiviral vector is another form of self-inactivating (SIN) vector as a result of a deletion in the 3' long terminal repeat region (LTR). Preferably, the vector contains a deletion within the viral promoter. The LTR of lentiviruses such as the HIV LTR contains a viral promoter. Although this promoter is relatively inefficient, when *trans*activated by e.g. tat, the promoter is relatively efficient. However, the presence of the viral promoter can interfere with heterologous promoters operably linked to a transgene. To minimize such interference and better regulate the expression of transgenes, the ~~lentiviral~~lentiviral promoter is preferably deleted.

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